

Figure 1

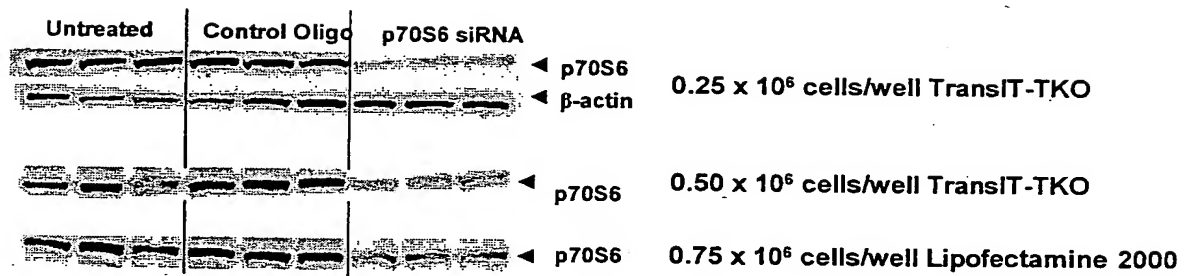


Figure 2

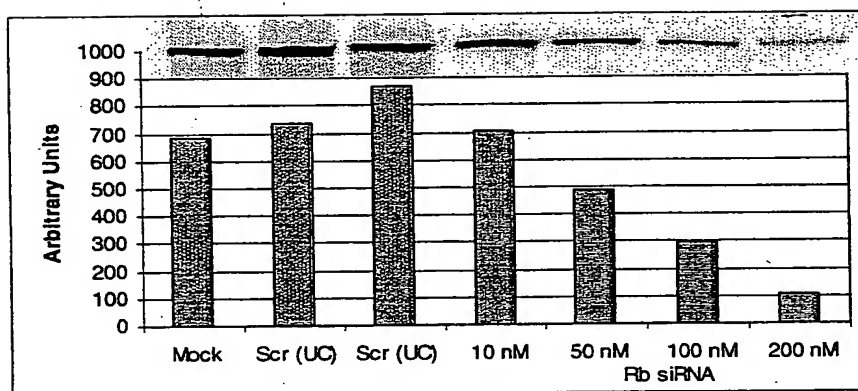


Figure 3

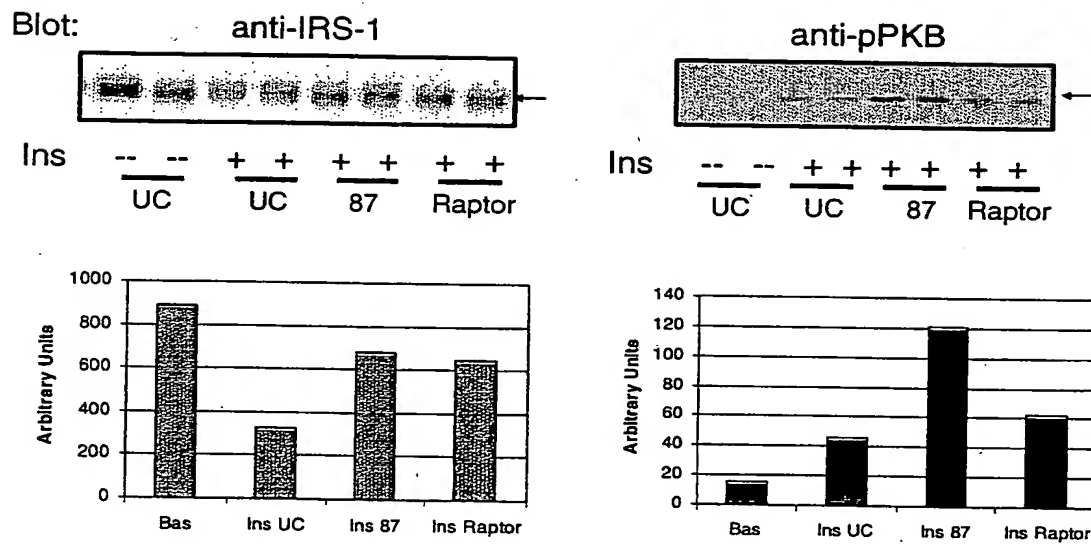


Figure 4

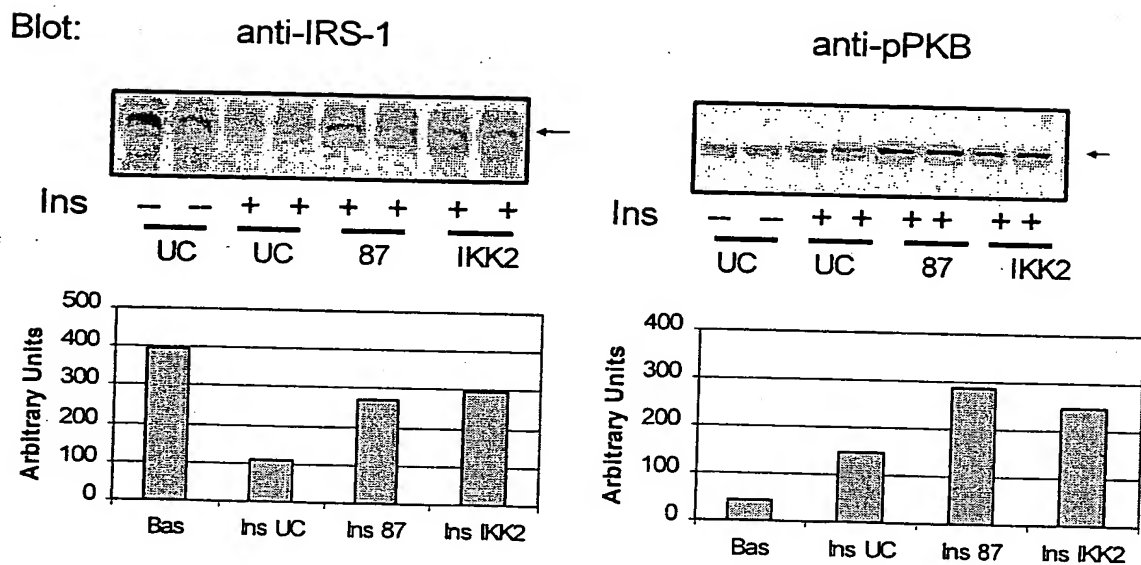


Figure 5

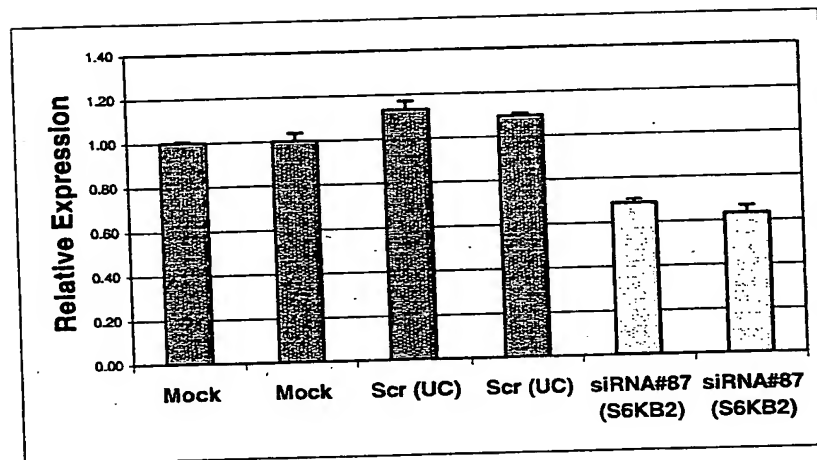


Figure 6

Blot:

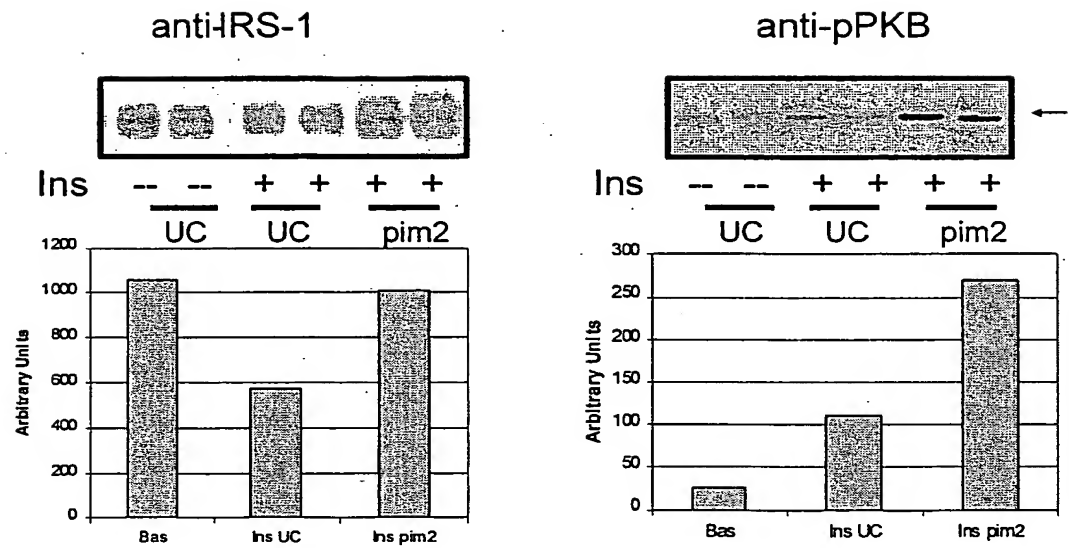


Figure 7

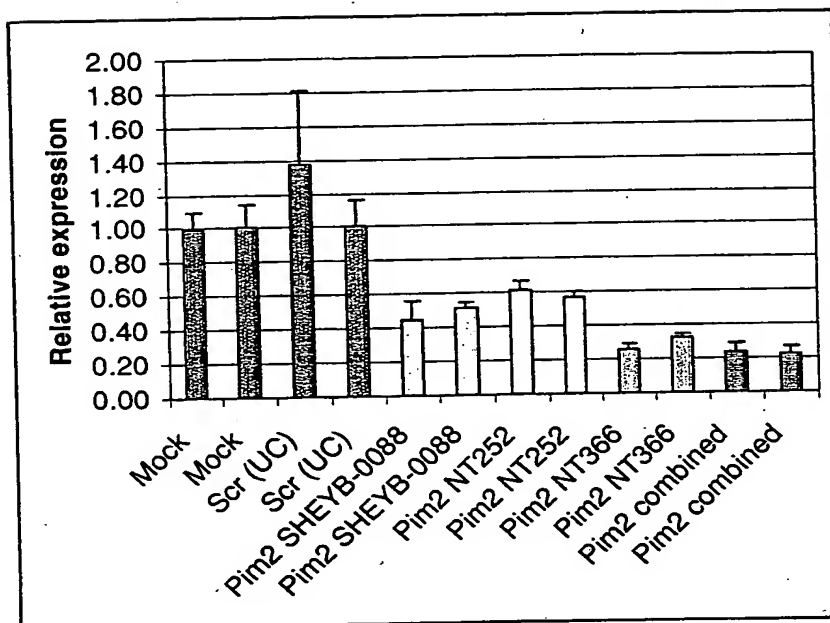
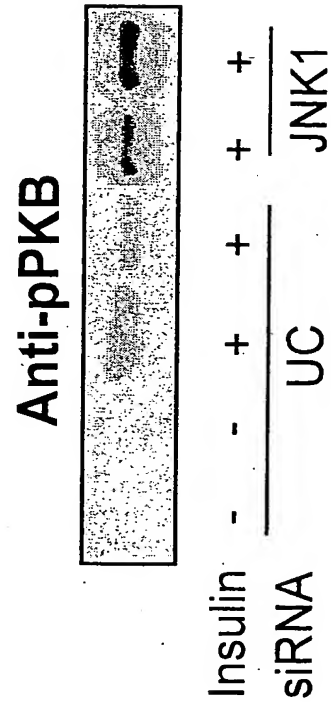
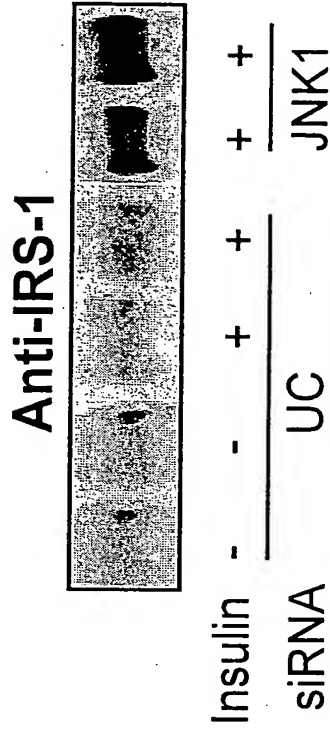
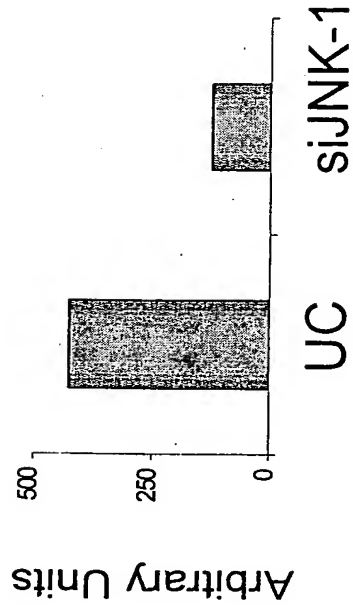


Figure 8

Fig. 9

Reduction of JNK-1 inhibits IRS-1 degradation and enhances insulin-induced PKB phosphorylation

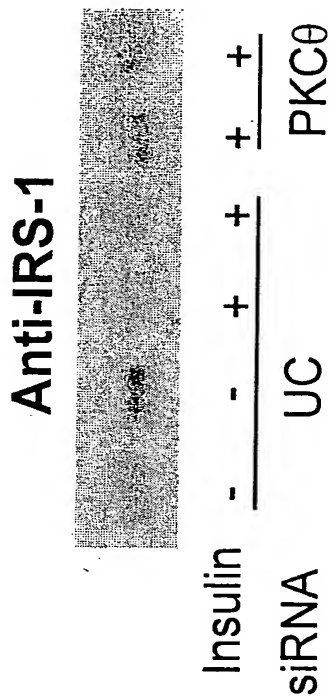
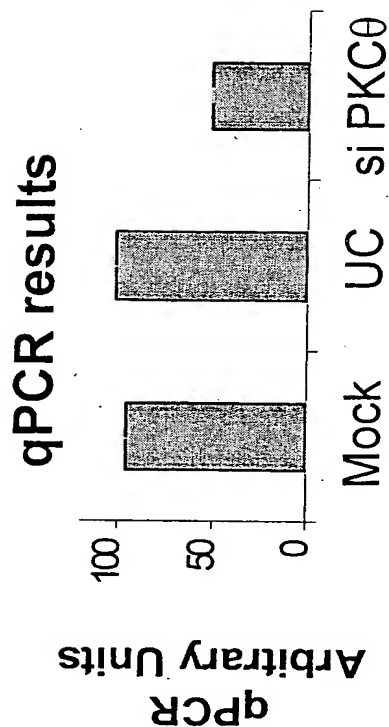
JNK-1 protein expression



- JNK activity is elevated in Type 2 diabetes and insulin resistance states
- JNK-1 -/- are protected to the development of diet induced obesity and insulin-resistance
- Reduction of JNK-1 in ob/ob mice improves insulin sensitivity and prevents diabetes

Fig. 10

Reduction of PKC θ inhibits IRS-1 degradation and enhances insulin-induced PKB phosphorylation



- FFA-induced insulin resistance is associated with activation of PKC θ
- PKC θ KO mice are protected from lipid induced insulin-resistance
- Increased PKC θ in muscle of patients with type 2 diabetes
- Chronic hyperinsulinemia increases PKC θ expression

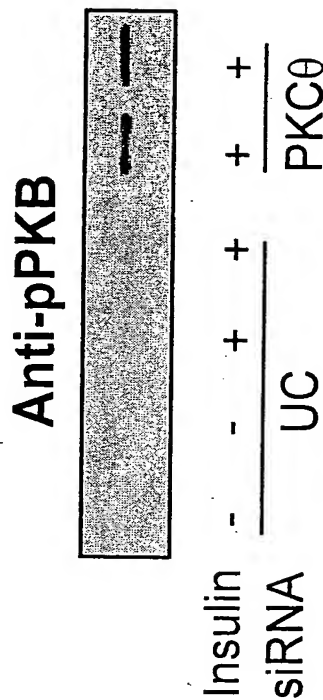
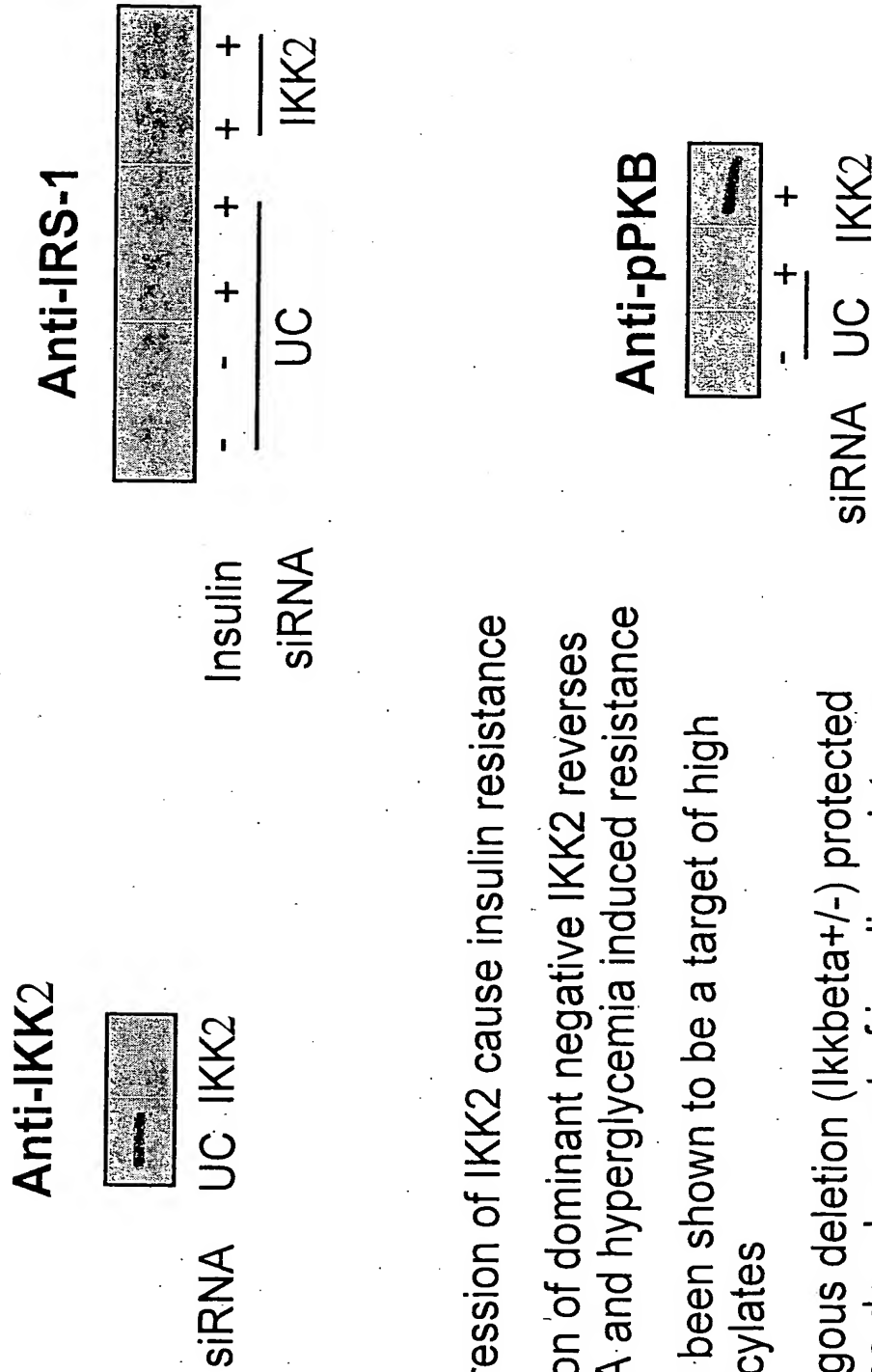


Fig. 11

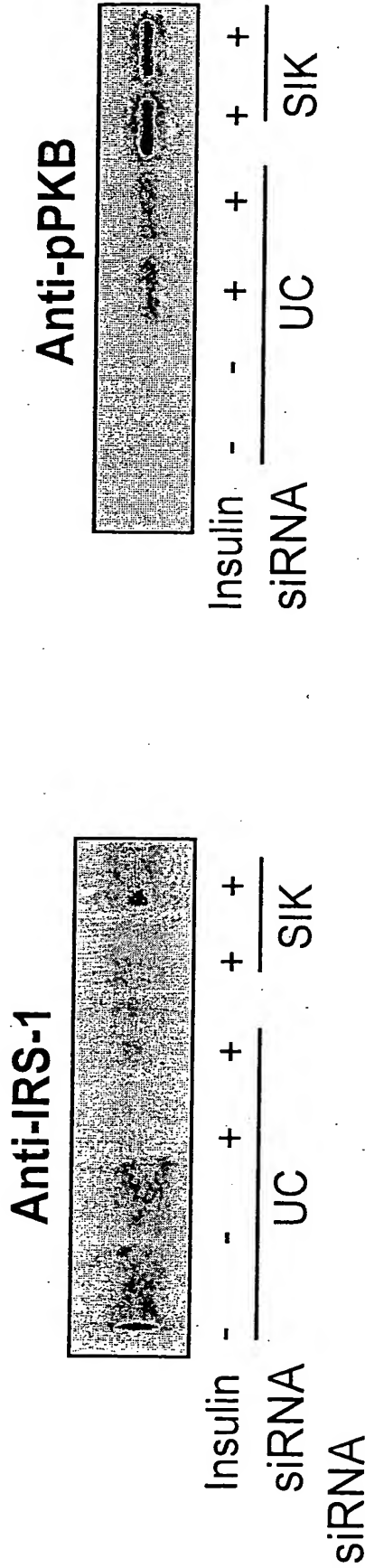
Reduction of IKK2 inhibits IRS-1 degradation and enhances insulin-induced PKB phosphorylation



- Overexpression of IKK2 cause insulin resistance
- Expression of dominant negative IKK2 reverses TNF, FFA and hyperglycemia induced resistance
- IKK2 has been shown to be a target of high dose salicylates
- Heterozygous deletion (Ikkbeta+/-) protected against the development of insulin resistance during high-fat feeding and in obese (ob/ob) mice

Fig. 12

Salt-inducible kinase-1 (SIK) is a new kinase involved in insulin resistance



- SIK was first cloned from the adrenal glands of rats fed a high salt diet
- Serine/threonine protein kinase that belongs to AMPK family
- SIK1 mRNA is elevated in adipose tissues, livers, and skeletal muscle of diabetic animals
- Involved in the phosphorylation of Ser⁷⁸⁹ in IRS-1 in livers of diabetic animals